REMARKS

Claims 1 to 4, and 6 to 12, and 15 to 21 are in the application. Claim 14 has been cancelled. Applicants reserve their right to file divisional or continuation applications on cancelled or deleted subject matter.

Rejection under 35 USC § 103

Claims 1 to 4 and 21 are rejected to under 35 USC § 103(a) as being unpatentable over Zirkle et al. (US Patent 2,800,478 ('478)) or Zirkle et al., J. Med. Chem. (1962) in view of Gillett et al., European Respiratory Journal (1988) and Sieger et al., US Patent 6,608,055 ('055). Applicant respectfully traverses this rejection.

Applicants thank the Examiner for including the text of the Gillett et al. Abstract over which they have been rejected.

The Examiner has not substantiated how a composition includes air. A composition includes a second component, be it a carrier or a diluent. Whether that 2nd component is a solid excipient or a liquid, such as water is not necessarily determined but it is a 2nd quantifiable component. The Examiner is request to point out where in US case law or the MPEP that air is a component of a composition.

A skilled artisan would readily understand that a compound suitable for use in an inhaled dosage form, e.g. a dry powder form used in oral inhalation requires some manipulation. The compound may require milling, and a suitable carrier to deliver the dosage amount to the lung tissues. Inhalant devices are quite complicated and so are the resulting spray patterns produced by the device. The compounds are often admixed with more than one carrier, and may include ternary agents as well. They are not administered "as air". US Patent 2,800,478 and the Zirkle et al. publication do NOT describe the compounds as being in a dry powder composition, which composition is suitable for inhalation therapy via the mouth. Again, it is also noted that an oral administration of a compound such as the Zirkle et al compounds may include carriers or excipients that are unacceptable for topical administration to the lung tissue as delivered dry powder inhalation.

The Examiner comments that the Zirkle et al. Med Chem. publication teaches the instant compound to be "active agents, equalling or exceeding atropine in potency". This is an in vitro assay that is discussed in the Zirkle et al. paper. The paper does not point out as previously agreed to by the Examiner what "tissues were involved", and the paper does not discuss the manner in which the compounds were tested *in vitro*. The testing of the compounds for activity is NOT a disclosure of a particular route of administration, e.g. inhalation by mouth to a human, nor a particular use of the compounds in vivo. However, what the Zirkle paper does substantiate is that some of the compounds of Zirkle et al. described in the paper are anticholinergics.

The Examiner cites Gillett et. al., for the preparation of an inhalable formulation of the compounds as "a trivial undertaking" and that it would be obvious to prepare a different formulation (a drug powder with additives, lactose, starch)" and test them per the teachings of Zirkle.

As previously discussed, Gillett teaches that methacholine chloride is administered by an aerosol. The Gillett abstract does not indicate how either the methacholine or the atropine was formulated. The abstract merely says that six asthmatic subjects were given increasing concentrations of methacholine aerosol which could be powder or liquid. The abstract also states that the subjects were premedicated with 0.9% sodium chloride (saline), or inhaled atropine at 4 different doses, or intravenous atropine. No formulation details are provided.

Atropine has a different structure than the instant compounds claimed herein. Metacholine chloride also has a different structure than the compounds claimed herein. Simply because a compound is known to have anticholinergic activity does not mean that the compound has the appropriate physical characteristics to be useful for administration as an INHALED compound. Most compounds are desired to be administered orally not topically to the lungs.

The compounds of the present invention are not 3-oxa-9-azoniatricyclo [3.3.1.0] derivatives, nor do then have an ester linkage off the nonane bridged ring (as in atropine). These characteristics produce compounds have differing chemical properties than the instantly claimed one. Absent an improper hindsight rejection, there is no reason to believe that the compounds of Zirkle et al. would actually have any utility as

an anticholinergic when administered to a patient topically to the lungs, via the inhaled route.

There is no motivation in any of these references to direct the skilled artisan to make a dry powder pharmaceutical formulation for inhaled use of the compounds of Zirkle. The '478 patent and the Med Chem. Articles of Zirkle do not teach nor suggest a pharmaceutical formulation, let alone a formulation for oral inhalation.

The teachings of Gillett et al. provide no disclosure or teaching which would direct the skilled artisan to formulate the presently claimed compounds for use as an inhaled compound, and the teaching of Sieger et al. are directed to a crystalline anhydrous form of an unrelated chemical compound. Consequently, the Examiner and the USPTO have failed to make out a *prima facie* case of obvious.

In view of these remarks, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 over Zirkle et al. is respectfully requested.

Rejection under 35 USC § 112

Claims 6 to 13 and 15 to 20 are rejected under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner has pointed out that the compounds of Zirkle are anticholinergic. Consequently utility has been satisfied.

"The enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003), citing *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). As noted, one of ordinary skill in the art would be able to synthesize a wide range of compounds of Formula (I) which are within the scope of the genus. This has been satisfied by the USPTO's allowance of the compounds of Formula (I) in US 2,800,478 of which the presently claimed compounds are a subset of.

Applicant's invention is the novel use of these compounds as a composition for delivery to the lungs, whether it is via the oral inhalation route or nasal delivery. The application provides a significant discussion on the various inhalers and formulation details therein. Consequently, it is believed that one of ordinary skill in the art is provided with sufficient information to also be able to use the compounds of Formula (I).

As noted, there may not even be a requirement to have any working embodiments in order to satisfy the requirements of § 112, first paragraph, even in the chemical arts, as evidenced by the decision in *In re Strahilevitz*, 668 F.2d 1229, 212 U.S.P.Q. 561 (CCPA 1982).

The nature of the applicants' invention itself would also not tend to cause one skilled in the art to doubt its usefulness.

As regards Applicants claimed subject matter, Claim 6 is a recitation that the composition (of Claim 1) inhibit the binding of acetylcholine to an acetylcholine receptor in a mammal. This method is not tied to the treatment of a particular disease state or respiratory condition as so noted by the Examiner, and is well supported in the specification.

The second binding assay, page 6, lines 16 to 24 provides for a pan muscarinic antagonism screening against the M1 to M5 acetylcholine receptors.

The skilled artisan would readily understand the significance of this assay and the potential limitations of compounds tested therein. This is a well known art recognized assay. The method of claim 6 does not require" treatment of a disease state". The claim limitations in Claim 6 are such that a compound of Formula (I) contact a particular receptor and that this contact is made by a route of administration, e.g. inhalation for receptors in the respiratory tract.

Claim 15 is drawn to very specific disease states which are known in the art to be treatable by M3 receptor antagonists. The breadth and scope of the claims herein are in fact limited to

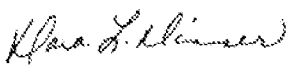
The specification provides for formulation details, amounts, how to use, and how to administer the claimed dry powder formulations of compounds of Formula (I), and reference additional patents on the various devices for such formulations.

It should be noted that previously disclose co-pending application 10/565,048 has been allowed with similar method claims to those contained herein.

In view of these remarks, reconsideration and withdrawal of the rejection to the claims is respectfully requested.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case, the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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